

TRAUMATIC BRAIN INJURY LEADS TO ABERRANT MIGRATION OF ADULT-BORN NEURONS IN THE HIPPOCAMPUS

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Traumatic brain injury (TBI) is the leading cause of death in children and young adults, leading to substantial cognitive impairment, motor dysfunction and epilepsy. There is no effective treatment for these disorders. The discovery of neural stem/progenitor cells (NSCs) in the adult brain raises a potentially promising strategy for repairing CNS injury. Our previous study showed that TBI promotes NSC proliferation in an attempt to initiate innate repair and/or plasticity mechanisms. However, the spontaneously post-traumatic recovery of hippocampal-related cognitive and memory functions is very limited. Better understanding of neurogenesis following TBI may provide additional intervention to further enhance neurogenesis for successfully repairing the damaged brain following TBI. Although newborn neurons generated from NSCs are continuously added to the brain throughout our life, they must migrate from their birthplace to their appropriate destination to develop into mature neurons. When we tracked the migration of newly generated neurons in the adult hippocampus after TBI, we found that a large percentage of immature neurons migrate past their normal stopping site at the inner granular cell layer, and misplace in the outer granular cell layer of the hippocampal dentate gyrus. The aberrant migration of adult-born neurons in the hippocampus occurs 3 days after TBI, and lasts for 10 weeks, resulting in a great number of newly generated neurons misplaced in the outer granular layer in the hippocampus. The newborn neurons at the displaced position will not be able to make correct connections with their appropriate targets, and may even make wrong connections with inappropriate nearby targets in the pre-existing neural network. Abnormal migration can cause several diseases including epilepsy. These results suggest that stimulation of endogenous adult neural stem cells following TBI might offer new avenues for cell-based therapy. Additional intervention is required to further enhance successful neurogenesis for repairing the damaged brain.

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